



**EXHIBIT A: MARKED VERSION OF AMENDED PARAGRAPHS IN THE  
SPECIFICATION**

U.S. APPLICATION SERIAL NO. 09/616,849  
(ATTORNEY DOCKET NO. 9301-044)

(as amended July 15, 2002)

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On page 1, please amend the paragraph beginning "This application claims priority to" as follows:

This application claims [priority to] the benefit of U.S. Provisional Patent Application Serial No. 60/144,382, filed on July 16, 1999 and U.S. Provisional Patent Application Serial No. 60/154,563, filed on September 17, 1999, each of which is incorporated by reference herein in its entirety.

On page 1, please amend the paragraph beginning "The field of this invention relates to the field" as follows:

The field of this invention relates to the field of detecting and reporting polynucleotide sequences, including genomic sequences, genomic transcript sequences (*e.g.*, mRNAs from cells and/or cDNA sequences derived therefrom) copy numbers and single nucleotide polymorphisms (SNPs), by nucleic acid hybridization, *e.g.*, on nucleic acid microarrays. In particular, the invention relates to methods for identifying and/or selecting polynucleotide sequences, particularly oligonucleotide sequences, which may be used as hybridization probes (*e.g.*, on nucleic acid microarrays) that are both [sensitivity] sensitive and specific to particular target polynucleotide sequences of interest.



EXHIBIT C: MARKED VERSION OF AMENDED CLAIMS

U.S. APPLICATION SERIAL NO. 09/616,849

(ATTORNEY DOCKET NO. 9301-044)

(as amended July 15, 2002)

27. (Twice Amended) A method for evaluating a binding [properties] property of a polynucleotide probe comprising a predetermined nucleotide sequence to a target nucleotide sequence, said method comprising comparing the amount of hybridization of polynucleotides in a first sample to the polynucleotide probe with the amount of hybridization of polynucleotides in a second sample to the polynucleotide probe, wherein:

- (a) the first sample comprises a plurality of polynucleotide molecules comprising said target nucleotide sequence; and
- (b) the second sample comprises a plurality of different polynucleotide molecules wherein each different polynucleotide molecule comprises a sequence that is different from the nucleotide sequences of any other polynucleotide molecules in said plurality of different polynucleotide molecules,

wherein [the first sample is] at least 75% [pure in] of the polynucleotide molecules in said first sample are polynucleotide molecules comprising said target nucleotide sequence, thereby evaluating said binding property of said polynucleotide probe.

33. (Twice Amended) The method of claim 27 wherein [the first sample is] at least 90% [pure in] of the polynucleotide molecules in said first sample are said polynucleotide molecules comprising said target nucleotide sequence.

34. (Twice Amended) The method of claim 33 wherein [the first sample is] at least 95% [pure in] of the polynucleotide molecules in said first sample are said polynucleotide molecules comprising said target nucleotide sequence.

35. (Twice Amended) The method of claim 34 wherein [in the first sample is] at least 99% [pure in] of the polynucleotide molecules in said first sample are said polynucleotide molecules comprising said target nucleotide sequence.

42. (Twice Amended) The method of claim [41] 40 wherein:

- (a) the target nucleotide sequence is a sequence of a gene or gene transcript of a cell or organism;
- (b) the first sample comprises a polynucleotide sample from a wild-type strain of the cell or organism which expresses the gene or gene transcript; and
- (c) the second sample comprises a polynucleotide sample from a deletion mutant of the cell or organism which does not express the gene or gene transcript.

48. (Amended) The method of claim 43 wherein the amount of each [different] polynucleotide molecule that does not comprise the target nucleotide sequence in the [plurality of different molecules of the] first sample differs from the amount of the corresponding [different] polynucleotide molecule in the plurality of different polynucleotide molecules of the second sample by no more than a factor of 100.

49. (Amended) The method of claim 43 wherein the amount of each [different] polynucleotide molecule that does not comprise the target nucleotide sequence in the [plurality of different molecules of the] first sample differs from the amount of the corresponding [different] polynucleotide molecule in the plurality of different polynucleotide molecules of the second sample by no more than a factor of 10.

50. (Amended) The method of claim 43 wherein the amount of each [different] polynucleotide molecule that does not comprise the target nucleotide sequence in the [plurality of different molecules of the] first sample differs from the amount of the corresponding [different] polynucleotide molecule in the plurality of different polynucleotide molecules of the second sample by no more than 50%.

51. (Amended) The method of claim 43 wherein the mean abundance of the [different] polynucleotide molecules that do not comprise the target nucleotide sequence in the [plurality of different polynucleotide molecules of the] first sample differs from the mean abundance of the different polynucleotide molecules in the plurality of different polynucleotide molecules of the second sample by no more than a factor of two.

52. (Amended) The method of claim 43 wherein the mean abundance of the [different] polynucleotide molecules that do not comprise the target nucleotide sequence in the [plurality of different polynucleotide molecules of the] first sample differs from the mean abundance of the different polynucleotide molecules in the plurality of different polynucleotide molecules of the second sample by no more than 50%.

53. (Amended) The method of claim 43 wherein the mean abundance of the [different] polynucleotide molecules that do not comprise the target nucleotide sequence in the [plurality of different polynucleotide molecules of the] first sample differs from the mean abundance of the different polynucleotide molecules in the plurality of different polynucleotide molecules of the second sample by no more than 10%.

54. (Amended) The method of claim 43 wherein the mean abundance of the [different] polynucleotide molecules in the [plurality of different polynucleotide molecules of the] first sample differs from the mean abundance of the different polynucleotide molecules in the plurality of different polynucleotide molecules of the second sample by no more than 1%.

Claims 55-56 have been canceled.

57. (Twice Amended) The method of claim 27 wherein said binding property is a specificity of the polynucleotide probe [is determined], wherein said specificity is the amount of said polynucleotide molecules comprising said target nucleotide sequence that bind to said polynucleotide probe relative to the amount of polynucleotide molecules not comprising said target nucleotide sequence that bind to the probe under the same binding conditions.

67. (Twice Amended) A method for evaluating a binding [properties] property of a plurality of polynucleotide probes to a target nucleotide sequence wherein each polynucleotide probe in the plurality of polynucleotide probes comprises a predetermined nucleotide sequence, said method comprising comparing the amount of hybridization of polynucleotides in a first sample to each polynucleotide probe in the plurality of polynucleotide probes with the amount of hybridization of polynucleotides in a second sample to each polynucleotide probe in

the plurality of polynucleotide probes, wherein:

- (a) the first sample comprises a plurality of polynucleotide molecules comprising said target nucleotide sequence; and
- (b) the second sample comprises a plurality of different polynucleotide molecules wherein each different polynucleotide molecule comprises a nucleotide sequence that is different from nucleotide sequence of any other polynucleotide molecules in said plurality of different polynucleotide molecules,

wherein [the first sample is] at least 75% [pure in] of the polynucleotide molecules in said first sample are polynucleotide molecules comprising said target nucleotide sequence, thereby evaluating said binding property of each said polynucleotide probe.

Claims 69-70 have been canceled.

71. (Twice Amended) The method of claim 67 wherein said binding property is a specificity of each polynucleotide probe in the plurality of different polynucleotide probes [is determined], wherein said specificity is the amount of said polynucleotide molecules comprising said target nucleotide sequence that bind to said polynucleotide probe relative to the amount of polynucleotide molecules not comprising said target nucleotide sequence that bind to the probe under the same binding conditions.

Claims 81-83 have been canceled.

New claim 90 has been added.